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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/730,964	12/08/2003	Frans J. Walther	13361.4010	5338

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EXAMINER	
MITRA, RITA	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 05/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/730,964	WALTHER ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment in response to office action dated August 9, 2005, filed on January 11, 2006 is acknowledged. Amendment to specification has been noted. New claims 28 and 29 have been added. Claims 20-29 are currently under consideration in the instant application.

Response to Amendment

Objection to Specification

The objections are withdrawn in response to amendment to specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20 and dependent claims 21-27 and claims 28, 29 remain/are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 20 encompasses a method for treating respiratory distress syndrome (RDS) comprising administering a pharmaceutically compatible composition comprised of a peptide analog of lung surfactant protein B comprising a dimer of a synthetic peptide from an N-terminal domain of animal lung surfactant protein B. In addition based on open language "comprising", the claimed polypeptide can have sequences added to the N-terminal or C-terminal end and any polypeptide or peptide, having an undefined structure.

Specification indicates at pages 18-19 that ...other N-terminal molecules may be created by truncation from the C-terminal end with preservation of the functional properties of surfactant protein B...therefore the invention contemplates molecules from between 25-77 residues, specifically, with

respect to alpha-helicity, other molecules having a length between 40 and 50 may yield a conformation preserving the function of the native SP-B protein. However, specification fails to demonstrate such N-terminal domain peptide analogs containing an amphipathic alpha-helical domain that retains the activity of Surfactant Protein B. However, this feature is not recited in the claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The specification fails to provide any description or demonstration of these analogs of the surfactant protein B that retains the activity of full length SP-B protein. The skilled artisan cannot envision the detailed chemical structure of the SP-B protein analog, Thus, Applicants' written description of the claimed invention is insufficient to show that the Applicants were in possession of the full scope of the claimed invention.

Claims 21-24 are drawn to a method of claim 20, wherein the pharmaceutical composition comprising a peptide analog of lung surfactant protein B comprising a dimer of a synthetic peptide from an N-terminal domain of mammalian lung surfactant protein B. Specification at page 9, lines 1-8 describes a generic formulation of the pharmaceutical compositions. However, there is no description about the specific element in the composition, for example "an animal-derived lung surfactant" of claim 21. Method claims 25-27 require a composition further comprising a phospholipid but specification fails to give the appropriate concentration of phospholipid and the active ingredient in the composition. Although, an *in vivo* experiment has been performed (page 19, Example 6) by using an animal model of Acute Respiratory Distress Syndrome. However, based on the result that the rats treated with SP-B1-25 dimer reached the highest oxygenation values would not determine whether the analog retains the biological activities of the native pulmonary surfactants.

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Claims 20-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling a method for treating RDS comprising administering a composition comprising a dimer of a synthetic peptide from an N-terminal domain of lung surfactant protein B, does not reasonably provide enablement for any peptide analog of lung surfactant protein B and a pharmaceutical composition containing this protein analog. The specification does not enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The factors most relevant to this rejection are: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 20-29 encompass a method for treating RDS comprising administration of a pharmaceutical composition comprising a peptide analog of lung surfactant protein B comprising a dimer of a synthetic peptide from an N-terminal domain of lung surfactant protein B. The specification, however, only discloses cursory conclusions, without data to support the findings that the synthetic peptide of the present invention mimics the active site of the SP-B protein and creates a synthetic analog of these amino acids to augment the properties of the native proteins (page 4, lines 10-13); that these covalently linked peptides form a dimer that mimics a portion of the secondary structure of native SP-B, thus retaining the biological activity of the native pulmonary surfactant (page 6, lines 14 –16). Furthermore, the specification at page 4, lines 17-18 indicates that SP-B1-25 dimer may replace or supplement full-length proteins currently used to treat RDS. There is no data indicating that a synthetic peptide analog of SP-B1-25 that mimics the active site of the SP-B protein and retains the properties of the native protein or a dimer that mimics a portion of the secondary structure of native SP-B, thus retaining the biological activity of the native pulmonary surfactant which can replace or supplement the full length SP-B protein. The specification indicates at pages 18-19 that ...other N-terminal molecules may be created by truncation from the C-terminal end with preservation of the functional properties of surfactant protein B...therefore the invention contemplates molecules from between 25-77 residues, specifically, with respect to alpha-helicity, other molecules having a length between 40 and 50 may yield a conformation preserving the function of the native SP-B protein. However, specification fails to demonstrate such N-terminal domain peptide analogs containing an amphipathic alpha-helical domain that retains the activity of Surfactant Protein B. Thus, undue experimentation would be required to practice the claimed peptide analogs.

Therefore, it is necessary to perform further experimentation to determine the biological properties of these dimers. Without such guidance, the experimentation left to those skilled in the art is undue.

In the instant case, the amount of experimentation is enormous since the number of changes from the specific sequence are large, one of skill in the art would have to make and test each one to determine if it had the lung surfactant protein B activity of the parent protein. The amount of guidance presented is limited to the exact sequence. No discussion is present as to where the changes might be made to the N-terminal domain of lung surfactant protein B. The nature of the invention is a method for treating RDS by administering a composition comprising of a new synthetic peptide sequence from N-terminal domain of lung surfactant protein B. The art is unpredictable. The effect of one or a few conservative substitutions might be somewhat predictable, if the active areas of the molecule were known, but more changes than that, are less predictable. The effect on function of this many changes is clearly unpredictable. Finally, these claims are very broad in the sense that many different proteins fall within the scope of the claims.

Based on this analysis, the finding of undue experimentation is mandated.

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20, 21, 24-27 and 29 are rejected under 35 USC 102 (b) as being anticipated by Waring et al. (Peptide Research, Vol. 2, No. 5, pp 308-313, 1989). Waring et al. teach synthetic amphipathic sequences of Surfactant Protein-B that duplicates effect of native pulmonary surfactant proteins. Peptidelipid mixtures approximate results found with native surfactant proteins both *in vitro* and *in vivo*. Effects found with native proteins or synthetic peptides include association with, and ordering of surfactant lipid (see abstract). The reference teaches synthesis of 2 peptide sequences SP-B1 (SP-B residues 15-25) and SP-B2 (SP-B residues 49-66), see col. 3, page 308; col. 1-3, page 309, Table 1 and

Fig. 1. The reference teaches preparation of peptide-lipid dispersions and labeling that with 1-palmitolyl-2-(5-doxyl stearoyl) phosphatidylcholine (claims 25-27). Further, Waring et al. teach an animal model assay system (col. 2, page 310) and tested the product in surfactant deficient rats. Their findings demonstrate that the mixture containing lipids with both SP-B1 and SP-B2 were associated with brisk improvements in oxygenation that approximated those found with bovine surfactant (see col. 3, page 311; Fig. 4; col. 2, page 12). Thus, Waring's pulmonary SP-Bs can be formulated for diseases states, wherein surfactant deficiency or inactivation is pathogenetic (claims 20, 21, 24-27, 29).

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita Mitra whose telephone number is 571-272-0954. The examiner can normally be reached on M-F, 10:00 am-7:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rita Mitra, Ph.D.
March 31, 2006

JON WEBER
SUPERVISORY PATENT EXAMINER